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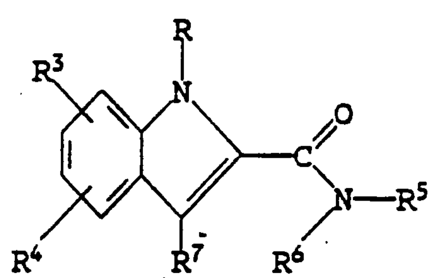

(I)

(57) Abstract

The invention relates to fungicidal compositions which comprise a carrier and, as active ingredient, an indole derivative of general formula (I), in which R represents a substituted phenyl group; R^3 and R^4 independently represent a hydrogen or a halogen atom or an optionally substituted alkyl, alkoxy, cycloalkyl, phenyl or phenoxy group; R^5 and R^6 independently represent a hydrogen atom or an optionally substituted alkyl, alkoxy, cycloalkyl, phenyl or heterocyclyl group or R^5 and R^6 together with the interjacent nitrogen atom represent a heterocyclyl group; and R^7 represents a hydrogen atom or an alkyl group; and their use as fungicides. Certain of the above mentioned indole derivatives are novel and a proces for the preparation of these compounds is also provided.

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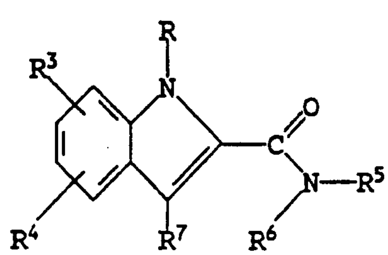
FUNGICIDAL INDOLE DERIVATIVES

The present invention relates to certain indole derivatives, processes for their preparation, compositions containing such compounds and their use as fungicides for the control of phytopathogenic fungi.

Indole derivatives having specific useful activities are well known. For instance, in French patent FR 2260332 certain 3-substituted derivatives of 1-phenyl-2-aminocarbonylindole having pharmaceutical activity are described. In German patent application DE 2008692 certain 3-aminocarbonylindole derivatives having herbicidal and pharmaceutical activity are described. From Japanese patent applications J5 0070357 and J5 0070358 1,3-disubstituted 2-aminoacetylindole derivatives and 1,3-disubstituted 2-(3-amino-propionyl)indole derivatives are known. These derivatives have antifungal as well as pharmaceutical activity. Additionally, DE 1966206 discloses 5-chloro-1-(2-fluorophenyl)-3-methyl-1H-indole-2-carboxamide as an intermediate in the preparation of certain 1,4-benzodiazepines which are useful as pharmaceuticals. There is no indication that this compound has any fungicidal activity.

It has now been found that certain new indole derivatives, especially indole derivatives which are unsubstituted at the 3-position, show excellent fungicidal activity, particularly against Phytophthora infestans and Plasmopora viticola.

According to the present invention there is therefore provided a fungicidal composition which comprises a carrier and, as active ingredient, a compound of the general formula



(I)

in which

R represents a substituted phenyl group;

R^3 and R^4 independently represent a hydrogen or halogen atom or an optionally substituted alkyl, alkoxy, cycloalkyl, phenyl or phenoxy group;

R^5 and R^6 independently represent a hydrogen atom or an optionally substituted alkyl, alkoxy, cycloalkyl, phenyl or heterocyclyl group or R^5 and R^6 together with the interjacent nitrogen atom represent a heterocyclyl group; and

R^7 represents a hydrogen atom or an alkyl group.

When the compounds in the compositions of this invention contain an alkyl or alkoxy substituent group, this may be linear or branched and may contain up to 12, preferably up to 6 and especially up to 4, carbon atoms. A cycloalkyl group may contain from 3 to 8, preferably 3 to 6, carbon atoms. A heterocyclyl group may be any saturated or unsaturated ring system containing at least one heteroatom, 3- to 6-membered rings being preferred and 5- and 6-membered rings being especially preferred. Nitrogen, oxygen- and sulphur-containing heterocyclic rings, such as pyrrolidine, pyrrole, pyrroline, pyrazole, imidazole, triazole, tetrazole, pyrazoline, pyridine, piperidine, dihydropyridazine, tetrahydropyridazine, pyrimidine, dihydropyrimidine, tetrahydropyrimidine, dihydropyrazine, tetrahydropyrazine, oxazoline, morpholine, dihydrothiazine, tetrahydrothiazine, piperazine, furan, pyran and thiophene, are particularly preferred.

When any of the foregoing substituents are designated as being optionally substituted, the substituent groups which are optionally present may be any one or more of those customarily employed in the development of pesticidal compounds and/or the modification of such compounds to influence their structure/activity, persistence, penetration or other property. Specific examples of such substituents include, for example, halogen atoms, nitro, cyano, hydroxyl, alkyl, haloalkyl, alkoxy, haloalkoxy, hydroxyalkyl, amino, alkylamino, dialkylamino, formyl, alkoxycarbonyl, carboxyl,

alkanoyl, alkylthio, alkylsulphinyl, alkylsulphonyl, carbamoyl, alkylamido, phenyl, phenoxy, benzyl, benzyloxy, alkylenedioxy and cycloalkyl, especially cyclopropyl, groups. Typically, 0-3 substituents may be present. When any of the foregoing substituents represents or contains an alkyl substituent group, this may be linear or branched and may contain up to 12, preferably up to 6, and especially up to 4, carbon atoms. When any of the foregoing substituents represents or contains a cycloalkyl moiety, the cycloalkyl moiety may itself be substituted by one or more halogen atoms, nitro, cyano, alkyl, haloalkyl, alkoxy or haloalkoxy groups. Generally, substituents of alkyl, alkenyl, cycloalkyl and phenyl groups are preferably halogen, methoxy, nitro, amino, cyano and, in the case of cycloalkyl and phenyl, also methyl and trifluoromethyl.

It is preferred that R represents a phenyl group substituted by one or more substituents selected from halogen atoms, nitro, cyano, hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, hydroxy-C_{1-4} alkyl, amino, C_{1-4} alkanoyl, carbamoyl and C_{1-4} alkylenedioxy groups.

More preferably, R represents a phenyl group substituted by one or more substituents selected from halogen atoms, nitro, cyano, hydroxyl, C_{1-4} alkyl, C_{1-4} alkoxy, hydroxy-C_{1-4} alkyl, amino, C_{1-4} alkanoyl, carbamoyl and C_{1-4} alkylenedioxy groups.

It is especially preferred that R represents a phenyl group substituted by one or two C_{1-4} alkoxy, especially methoxy or ethoxy, groups. Most preferably, R represents a 3,4-dimethoxyphenyl group.

Preferably, R^3 and R^4 independently represent a hydrogen or halogen atom, an optionally substituted C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-8} cycloalkyl, phenyl or phenoxy group.

It is preferred that R^3 and R^4 independently represent a hydrogen or halogen atom or a C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-8} cycloalkyl, phenyl or phenoxy group, each group being optionally substituted by one or more substituents selected from halogen atoms and phenyl groups.

More preferably, R^3 and R^4 independently represent a hydrogen or halogen atom or a C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-6} cycloalkyl, phenyl or phenoxy group, each group being optionally substituted by one or more substituents selected from halogen, especially fluorine and chlorine, atoms and phenyl groups.

Even more preferably, R^3 and R^4 independently represent a hydrogen, fluorine or chlorine atom, a C_{1-4} alkyl group or a C_{1-4} alkoxy group. It is especially preferred that R^4 is a hydrogen atom and R^3 is a hydrogen, fluorine or chlorine atom or a C_{1-4} alkyl group, R^3 even more preferably being a hydrogen atom, a 5- or 6-chloro atom or a n-C_{1-4} alkyl group, substitution at the 5-position being especially preferred.

Preferably, R^5 and R^6 independently represent a hydrogen atom, a C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-8} cycloalkyl or phenyl group or a 5- to 6- membered heterocyclic ring or R^5 and R^6 together with the interjacent nitrogen atom represent a 5- to 6- membered heterocyclic ring, each group or ring being optionally substituted by one or more substituents selected from halogen atoms, C_{3-6} cycloalkyl, halo-C_{3-6} cycloalkyl and phenyl groups.

More preferably, R^5 and R^6 independently represent a hydrogen atom, a C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-6} cycloalkyl, phenyl or morpholinyl group or R^5 and R^6 together with the interjacent nitrogen atom represent an imidazolyl, piperidyl or morpholinyl group, each group being optionally substituted by one or more substituents selected from halogen, especially fluorine and chlorine, atoms, cyclopropyl, dichlorocyclopropyl and phenyl groups.

It is particularly preferred that R^5 and R^6 together with the interjacent nitrogen atom represent a piperidyl or morpholinyl group, each group being optionally substituted by one or two halogen, especially fluorine, atoms. Most preferably, R^5 and R^6 together with the interjacent nitrogen atom represent a morpholinyl group.

It is also preferred that R^7 represents a hydrogen atom or a C_{1-4} alkyl, especially a methyl, group. It is especially preferred

that R^7 represents a hydrogen atom.

A particulary preferred sub-group of compounds of formula I is that in which R represents a nitrophenyl, cyanophenyl, hydroxyphenyl, hydroxymethylphenyl, aminophenyl, ethanoylphenyl, carbamoylphenyl, methylenedioxyphenyl, fluoro-methyl-phenyl, fluoro-methoxy-phenyl, fluoro-amino-phenyl, difluoro-amino-phenyl, chloro-amino-phenyl, dichloro-amino-phenyl, hydroxyl-methoxy-phenyl, methyl-methoxy-phenyl, methyl-amino-phenyl, ethyl-amino-phenyl or dimethoxyphenyl group; R^3 represents a hydrogen, fluorine, chlorine or bromine atom or a methyl, ethyl, propyl, butyl, trifluoromethyl, methoxy, ethoxy, propoxy, butoxy, benzyloxy, cyclohexyl, phenyl or chlorophenoxy group; R^4 represents a hydrogen atom; R^5 represents a methyl, ethyl, propyl, butyl, trifluoroethyl, cyanomethyl, dichlorocyclopropylmethyl, benzyl, methoxy, cyclopropyl, cyclohexyl, phenyl or morpholinyl group; R^6 represents a hydrogen atom or a methyl, ethyl or propyl group; or R^5 and R^6 together with the interjacent nitrogen atom represent an imidazolyl, piperidyl or morpholinyl group; and R^7 represents a hydrogen atom or a methyl group.

A method of making a composition as defined above is also provided which comprises bringing a compound of formula I as defined above into association with at least one carrier. Such a composition may contain a single compound or a mixture of several compounds of the invention.

A composition according to the invention preferably contains from 0.5 to 95% by weight of active ingredient.

A carrier in a composition according to the invention is any material with which the active ingredient is formulated to facilitate application to the locus to be treated, which may for example be a plant, seed or soil, or to facilitate storage, transport or handling. A carrier may be a solid or a liquid, including a material which is normally gaseous but which has been compressed to form a liquid, and any of the carriers normally used in formulating fungicidal compositions may be used.

Suitable solid carriers include natural and synthetic clays and silicates, for example natural silicas such as diatomaceous earths; magnesium silicates, for example talcs; magnesium aluminium silicates, for example attapulgites and vermiculites; aluminium silicates, for example kaolinites, montmorillonites and micas; calcium carbonate; calcium sulphate; ammonium sulphate; synthetic hydrated silicon oxides and synthetic calcium or aluminium silicates; elements, for example carbon and sulphur; natural and synthetic resins, for example coumarone resins, polyvinyl chloride, and styrene polymers and copolymers; solid polychlorophenols; bitumen; waxes, for example beeswax, paraffin wax, and chlorinated mineral waxes; and solid fertilisers, for example superphosphates.

Suitable liquid carriers include water; alcohols, for example isopropanol and glycols; ketones, for example acetone, methyl ethyl ketone, methyl isobutyl ketone and cyclohexanone; ethers; aromatic or araliphatic hydrocarbons, for example benzene, toluene and xylene; petroleum fractions, for example, kerosine and light mineral oils; chlorinated hydrocarbons, for example carbon tetrachloride, perchloroethylene and trichloroethane. Mixtures of different liquids are often suitable.

Fungicidal compositions are often formulated and transported in a concentrated form which is subsequently diluted by the user before application. The presence of small amounts of a carrier which is a surface-active agent facilitates this process of dilution. Thus preferably at least one carrier in a composition according to the invention is a surface-active agent. For example the composition may contain at least two carriers, at least one of which is a surface-active agent.

A surface-active agent may be an emulsifying agent, a dispersing agent or a wetting agent; it may be nonionic or ionic. Examples of suitable surface-active agents include the sodium or calcium salts of polyacrylic acids and lignin sulphonic acids; the condensation products of fatty acids or aliphatic amines or amides containing at least 12 carbon atoms in the molecule with ethylene oxide and/or propylene oxide; fatty acid esters of glycerol,

sorbitol, sucrose or pentaerythritol; condensates of these with ethylene oxide and/or propylene oxide; condensation products of fatty alcohol or alkyl phenols, for example p-octylphenol or p-octylcresol, with ethylene oxide and/or propylene oxide; sulphates or sulphonates of these condensation products; alkali or alkaline earth metal salts, preferably sodium salts, of sulphuric or sulphonic acid esters containing at least 10 carbon atoms in the molecule, for example sodium lauryl sulphate, sodium secondary alkyl sulphates, sodium salts of sulphonated castor oil, and sodium alkylaryl sulphonates such as dodecylbenzene sulphonate; and polymers of ethylene oxide and copolymers of ethylene oxide and propylene oxide.

The compositions of the invention may for example be formulated as wettable powders, dusts, granules, solutions, emulsifiable concentrates, emulsions, suspension concentrates and aerosols. Wettable powders usually contain 25, 50 or 75% w of active ingredient and usually contain in addition to solid inert carrier, 3-10% w of a dispersing agent and, where necessary, 0-10% w of stabiliser(s) and/or other additives such as penetrants or stickers. Dusts are usually formulated as a dust concentrate having a similar composition to that of a wettable powder but without a dispersant, and may be diluted in the field with further solid carrier to give a composition usually containing ½-10% w of active ingredient. Granules are usually prepared to have a size between 10 and 100 BS mesh (1.676 - 0.152 mm), and may be manufactured by agglomeration or impregnation techniques. Generally, granules will contain ½-75% w active ingredient and 0-10% w of additives such as stabilisers, surfactants, slow release modifiers and binding agents. The so-called "dry flowable powders" consist of relatively small granules having a relatively high concentration of active ingredient. Emulsifiable concentrates usually contain, in addition to a solvent and, when necessary, co-solvent, 1-50% w/v active ingredient, 2-20% w/v emulsifiers and 0-20% w/v of other additives such as stabilisers, penetrants and corrosion inhibitors. Suspension concentrates are usually

compounded so as to obtain a stable, non-sedimenting flowable product and usually contain 10-75% w active ingredient, 0.5-15% w of dispersing agents, 0.1-10% w of suspending agents such as protective colloids and thixotropic agents, 0-10% w of other additives such as defoamers, corrosion inhibitors, stabilisers, penetrants and stickers, and water or an organic liquid in which the active ingredient is substantially insoluble; certain organic solids or inorganic salts may be present dissolved in the formulation to assist in preventing sedimentation or as anti-freeze agents for water.

Aqueous dispersions and emulsions, for example compositions obtained by diluting a wettable powder or a concentrate according to the invention with water, also lie within the scope of the invention. The said emulsions may be of the water-in-oil or of the oil-in-water type, and may have a thick 'mayonnaise' like consistency.

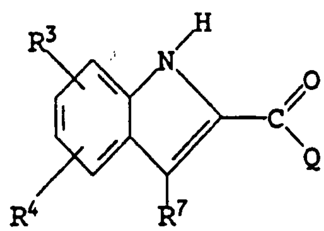
The composition of the invention may also contain other ingredients, for example other compounds possessing herbicidal, insecticidal or fungicidal properties.

Of particular interest in enhancing the duration of the protective activity of the compounds of this invention is the use of a carrier which will provide a slow release of the fungicidal compounds into the environment of the plant which is to be protected. Such slow-release formulations could, for example, be inserted in the soil adjacent to the roots of a vine plant, or could include an adhesive component enabling them to be applied directly to the stem of a vine plant.

The present invention still further provides the use as a fungicide of a compound of the general formula I as defined above or a composition as defined above, and a method for combating fungus at a locus, which comprises treating the locus, which may be for example plants subject to or subjected to fungal attack, seeds of such plants or the medium in which such plants are growing or are to be grown, with such a compound or composition.

Certain of the compounds of formula I as defined above are novel. Accordingly, the invention also provides a compound of the general formula I as previously defined with the proviso that, when R represents a 2-fluorophenyl group, R^2, R^4, R^5 and R^6 each represent a hydrogen atom and R^7 represents a methyl group, then R^3 does not represent a chlorine atom substituted at the 5-position of the indole ring.

The present invention also provides a process for the preparation of a compound of the general formula I as defined above which comprises reacting a compound of the general formula



(II)

in which R^3, R^4 and R^7 are as defined above and Q represents a group $-NR^5R^6$ or a group $-OR^8$ where R^5 and R^6 are as defined above and R^8 represents an alkyl or alkenyl group, with a compound of the general formula

$$R\text{—}Hal \qquad \text{(III)}$$

in which R is as defined above and Hal represents a halogen atom; and, when Q represents a group $-OR^8$ in the compound of formula II, reacting the compound so obtained with a compound of the general formula

$$HNR^5R^6 \qquad \text{(IV)}$$

in which R^5 and R^6 are as defined above.

The conversion of the compound obtained by reaction of a compound with the general formula II in which Q represents a group

$-OR^8$ and a compound of the general formula III comprises hydrolysis of the ester and, preferably, activation of the acid so obtained using an activating agent, followed by the reaction of the activated intermediate with an amine of the general formula IV. The activating agent is preferably N,N'-carbonyldiimidazole or an ester of chloroformic acid, e.g a C_{1-4} alkyl ester. Another possibility is the direct conversion of the ester with the amine of the general formula IV under the influence of a catalyst, e.g. a strong base, such as, for instance, sodium or potassium alcoholates such as sodium methoxide. R^8 preferably represents a C_{1-6} alkyl group.

The first step of the preparation process, which process as such is known in the art, see for instance H. Ishi et al, Chem. Pharm. Bull., 39, 572-578 (1991), is carried out by reaction of an appropriately substituted indole-2-carboxylic ester or amide of the formula II with an appropriately substituted aromatic halide of the formula III in the presence of a suitable catalyst. Suitable catalysts are salts of transition elements in which the valence of the element is not the maximum value, especially copper salts. Preferably halides are used, especially copper(I) bromide. In order to neutralise the hydrogen halide which is formed during the reaction, suitably a base is added to the reaction mixture. Very suitably carbonates or bicarbonates derived from alkali metals or alkaline earth metals are used. Further, organic bases, such as pyridine, may be added to the reaction mixture. The reaction is carried out in an inert organic solvent, e.g. aromatic solvents, especially nitrobenzene, toluene and xylene, at elevated temperatures. The temperature is suitably between 40 and 180 °C, preferably between 100 and 140 °C.

The product is isolated and optionally purified, whereafter, if necessary, the ester group is converted into the amide group by hydrolysis followed by reaction with the appropriate amine, suitably after activation of the acid. Activation is suitably carried out by reaction with activating reagents, for instance chlorinating or brominating agents, such as phosphorus oxychloride, thionyl chloride and sulphuryl chloride, N,N'-carbonyldiimidazole

or esters of chloroformic acid. Direct conversion under the influence of a basic catalyst is also possible. The hydrolysis reaction suitably may be carried out in a protic solvent, for instance a mixture of an alcohol and water. Acid or base may be added to improve the reaction rate. After isolation and drying of the product, optionally followed by purification, the product is reacted with the activating agent under reaction conditions well known in the art, whereafter the activated product is reacted with the appropriate amine compound, also at reaction conditions well known in the art.

In the case where the starting product of the general formula II is a carboxylic amide compound it will be appreciated that this compound may be obtained by reaction of the corresponding ester in the same way as described hereinbefore.

Compounds of formula II in which Q is $-OR^8$ and compounds of formulae III and IV are known compounds or can be prepared by processes analogous to known processes.

The present invention is of wide applicability in the protection of crop plants against fungal attack. Typical crops which may be protected include vines, potatoes, tomatoes, tobacco, hops, salads and cucumber. The duration of protection is normally dependent on the individual compound selected, and also a variety of external factors, such as climate, whose impact is normally mitigated by the use of a suitable formulation.

The invention is further illustrated by the following examples.

<u>Example 1</u>

<u>Preparation of 1-(3,4-dimethoxyphenyl)indole-2-carboxylic acid morpholide</u>

<u>(R=3,4-$(OCH_3)_2$phenyl; R^3=R^4=R^7=H; $-NR^5R^6$=morpholin-4-yl)</u>

(a) <u>Preparation of 1-(3,4-dimethoxyphenyl)indole-2-carboxylic acid ethyl ester</u>

4-Bromoveratrole (8.8 g, 40 mmol), indole-2-carboxylic acid ethyl ester (1.9 g, 10 mmol), potassium carbonate (1.9 g),

copper-(I)bromide (0.2 g), pyridine (2 ml) and nitrobenzene (10 ml) were stirred at 140°C for 14 hours. After cooling to room temperature, the reaction mixture was applied onto a silica gel flash chromatography column (silica gel: 140 g). The column was subsequently eluted with toluene (500 ml), toluene/acetone (95:5, 500 ml) and toluene/acetone (90:10, 500ml). 1-(3,4-Dimethoxyphenyl)indole-2-carboxylic acid ethyl ester was eluted with toluene/acetone (90:10) and gave colourless crystals upon evaporation of the solvent. The crystals were triturated with diisopropyl ether, collected by vacuum filtration and dried in the air. Yield: 3.0 g (92% of theoretical yield) M.pt.: 126-128°C. R_f (toluene/acetone, 9:1) = 0.53.

(b) <u>Preparation of 1-(3,4-dimethoxyphenyl)indole-2-carboxylic acid</u>

1-(3,4-Dimethoxyphenyl)indole-2-carboxylic acid ethyl ester (2.5 g, 7.7 mmol) obtained in (a) above and potassium hydroxide (0.6 g, 10 mmol) in water (5 ml) and ethanol (10 ml) were refluxed for 3 hours. The solvent was then removed by evaporation and the residue dissolved in a small amount of water. 1-(3,4-Dimethoxyphenyl)indole-2-carboxylic acid was precipitated as colourless amorphous material by dropwise addition of hydrochloric acid (5 M), chilled to 10°C, collected by vacuum filtration and dried at 90°C for 5 hours. Yield: 2.2 g (96% of theoretical) M.pt.: 240-245°C.

(c) <u>Preparation of 1-(3,4-Dimethoxyphenyl)indole-2-carboxylic acid morpholide (compound 1)</u>

1-(3,4-Dimethoxyphenyl)indole-2-carboxylic acid (2.2 g, 7.4 mmol) obtained in (b) above was stirred in tetrahydrofuran (15 ml) and N,N'-carbonyl- diimidazole (2.4 g, 15 mmol) was added whereupon a clear solution developed. The solution was refluxed for 30 minutes. After the solution had cooled to 20°C, morpholine (0.7 g, 8 mmol) was added dropwise and the reaction mixture first stirred at room temperature for 10 minutes, then under reflux for 30 minutes. The solvent was evaporated, the residue dissolved in toluene and washed twice with water. The organic layer was

evaporated and the residue applied onto a flash chromatography column packed with silica gel (30 g). The column was subsequently eluted with toluene/acetone (9:1, 250 ml) and toluene/acetone (8:2, 250 ml). 1-(3,4-Dimethoxyphenyl)indole-2-carboxylic acid morpholide was eluted with toluene/acetone (8:2) and gave a colourless viscous oil after evaporation of the solvent.
Yield: 2.4 g (88.6% of theoretical) R_f(toluene/acetone, 7:3) = 0.43 ^{1}H-NMR ($CDCl_3$): δ(ppm)= 7.7 (d; 1H), 7.4 (d; 1H), 7.1-7.3 (m; 2H), 7.0 (m; 1H), 7.0 (m; 2H), 6.8 (s; 1H), 3.95 (s; 3H), 3.90 (s; 3H), 3.2-3.8 (b; 8H).

Examples 2 to 78

By processes similar to those described in Example 1 above, further compounds according to the invention may be prepared as detailed in Table 1 below. In this table the compounds are identified by reference to formula I. Melting point and ^{1}H-NMR spectroscopy data are given in Table IA below in which the compounds are identified by reference to the Example numbers.

TABLE 1

(NB. In all the following examples R^4=H)

Ex. No.	R	R^3	$-NR^5R^6$	R^7
2	3,4-$(OCH_3)_2$ phenyl	H	imidazol-1-yl	H
3	"	H	$-NH-{}^iC_3H_7$	"
4	"	H	$-NH-C_6H_5$	"
5	"	H	$-NH-{}^nC_4H_9$	"
6	"	H	$-NH-CH_3$	"
7	"	H	$-N(CH_3)-CH_2C_6H_5$	"
8	"	5-Cl	morpholin-4-yl	"
9	"	6-Cl	"	"
10	"	5-Br	"	"

Table 1 (cont'd)

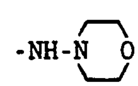
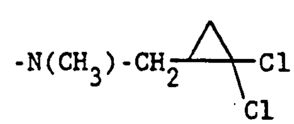
Ex. No.	R	R^3	$-NR^5R^6$	R^7
11	3,4-$(OCH_3)_2$ phenyl	6-CF_3	morpholin-4-yl	H
12	"	6-CH_3	"	"
13	"	5-$^nC_4H_9$	"	"
14	"	5-$O^nC_4H_9$	"	"
15	"	5-$O^nC_3H_7$	"	"
16	"	5-C_6H_5	"	"
17	"	5-O(4-Cl phenyl)	"	"
18	"	H	$-N(CH_3)_2$	"
19	"	H	$-N(CH_3)-C_2H_5$	"
20	"	H	$-N(C_2H_5)_2$	"
21	"	H	$-N(CH_3)-{}^nC_3H_7$	"
22	"	H	$-N(CH_3)-{}^nC_4H_9$	"
23	"	H	piperid-1-yl	"
24	"	5-CH_3	morpholin-4-yl	"
25	"	5-CH_3	$-N(C_2H_5)_2$	"
26	"	5-CH_3	$-N(CH_3)-{}^nC_3H_7$	"
27	"	5-CH_3	$-N({}^nC_3H_7)_2$	"
28	"	H	$-N(C_2H_5)-{}^iC_3H_7$	"
29	"	H	$-N(CH_3)-CH_2CN$	"
30	"	H	$-N(CH_3)OCH_3$	"
31	"	H		"
32	"	H	$-N(CH_3)-CH(CH_3)C_2H_5$	"
33	"	H		"
34	"	H	$-NHCH_2CF_3$	"
35	"	5-$^nC_4H_9$	$-N(C_2H_5)_2$	"

Table 1 (cont'd)

Ex. No.	R	R^3	$-NR^5R^6$	R^7
36	3,4-$(OCH_3)_2$ phenyl	5-F	morpholin-4-yl	H
37	"	5-F	$-N(C_2H_5)_2$	"
38	"	5-C_2H_5	morpholin-4-yl	"
39	"	5-C_2H_5	$-N(C_2H_5)_2$	"
40	"	5-OC_2H_5	$-N(C_2H_5)_2$	"
41	"	H	$-N(OCH_3)C_2H_5$	"
42	"	5-$C(CH_3)_3$	morpholin-4-yl)	"
43	"	5-$C(CH_3)_3$	$-N(C_2H_5)_2$	"
44	"	H	$-N(C_2H_5)$-cyclohexyl	"
45	"	cyclohexyl	morpholin-4-yl	"
46	"	cyclohexyl	$-N(C_2H_5)_2$	"
47	"	H	-NH-cyclopropyl	"
48	"	H	$-N(C_2H_5)$-cyclopropyl	"
49	"	H	$-N(CH_3)$-cyclopropyl	"
50	"	H	$-N(C_2H_5)-{}^nC_3H_7$	"
51	"	H	$-N(C_2H_5)-{}^nC_4H_9$	"
52	"	5-OCH_3	morpholin-4-yl	"
53	"	5-OCH_3	$-N(C_2H_5)_2$	"
54	"	5-$CH(CH_3)_2$	$-N(C_2H_5)_2$	"
55	"	5-$CH(CH_3)_2$	morpholin-4-yl	"
56	"	5-Cl	$-N(C_2H_5)_2$	"
57	"	5-$OCH_2C_6H_5$	morpholin-4-yl	"
58	"	5-$OCH_2C_6H_5$	$-N(C_2H_5)_2$	"
59	"	H	$-N(CH_3)-{}^iC_3H_7$	"
60	3,5-Cl_2,4-NH_2 phenyl	"	morpholin-4-yl	"
61	3-OCH_3,4-OH phenyl	"	"	"
62	3,4-OCH_2O- phenyl	"	"	"
63	3-CH_3,4-OCH_3 phenyl	"	"	"
64	3-Cl,4-NH_2 phenyl	"	"	"

Table 1 (cont'd)

Ex. No.	R	R^3	$-NR^5R^6$	R^7
65	3-F,4-NH_2 phenyl	H	morpholin-4-yl	H
66	4-NH_2 phenyl	"	"	"
67	3-F,4-CH_3 phenyl	"	"	"
68	3,5-F_2,4-NH_2 phenyl	"	"	"
69	4-$CONH_2$ phenyl	"	"	"
70	4-$COCH_3$ phenyl	"	"	"
71	3-C_2H_5,4-NH_2 phenyl	"	"	"
72	4-OH phenyl	"	"	"
73	3-F,4-OCH_3 phenyl	"	"	"
74	4-CN phenyl	"	"	"
75	4-CH_2OH phenyl	"	"	"
76	4-NO_2 phenyl	"	"	"
77	3,4-$(OCH_3)_2$ phenyl	"	"	$-CH_3$
78	3-CH_3,4-NH_2 phenyl	"	"	H

Table 1A

Ex. No.	M.pt (°C)	^{1}H-NMR δ (ppm)
2	oil	8.55(s;1H), 7.95(d;1H), 7.88(s;1H), 7.62(s;1H), 7.56-7.26(m;4H), 7.26-7.03(m;3H), 3.93(s;3H), 3.85(s;3H)
3	oil	7.67(d;1H), 7.28-7.07(m;4H), 6.98(m;2H), 6.87(d;1H), 5.62(br d;1H), 4.13(m;1H), 3.95(s;3H), 3.84(s;3H), 1.07(d;6H)
4	oil	7.71(d;1H), 7.40-7.03(m;4H), 7.00(m;2H), 6.93(d;1H), 4.96(s;3H), 4.83(s;3H)

Table 1A (cont'd)

Ex. No.	M.pt (°C)	^{1}H-NMR δ(ppm)
5	oil	7.68(d;1H), 7.38-7.07(m;4H), 6.98(m;2H), 6.87(d;1H), 5.80(br t;1H), 3.95(s;3H), 3.83(s;3H), 3.30(q;2H), 1.40(m;2H), 1.22(m;2H), 0.87(t;3H)
6	oil	7.65(d;1H), 7.32-7.04(m;4H), 6.98-6.85(m;3H), 6.10(br q; 1H), 3.95(s;3H), 3.83(s;3H), 2.85(d,3H)
7	oil	7.72-6.75(m;13H), 4.60, 4.50(2br s;2H), 3.98(s;3H), 3.80(s;3H), 2.87,2.78(2br s;3H)
8	170-175	7.7(m;7H), 3.95(s;3H), 3.88(s;3H), 3.75-3.15(br m;8H)
9		7.6(d;1H), 7.3(s;1H), 7.15(d;1H), 7.0(m;2H), 6.9(s;1H), 6.7(s;1H), 4.0(s;3H), 3.9(s;3H), 3.7-3.2(br;8H)
13		7.48-6.7(m;7H), 3.95(s;3H), 3.88(s;3H), 3.8-3.1(br.m;9H), 2.75-2.65(t;2H), 1.7-1.5(m;2H), 1.48-1.3(m;2H), 1.0-0.85(t;3H)
18	oil	7.7-6.7(m;8H), 3.95(s;3H), 3.87(s;3H), 3.0-2.8(br d;6H)
19	oil	7.70(d;1H), 7.45(d;1H), 7.3-7.15(m;2H), 7.05-6.90(m;3H), 6.7(br;1H), 4.0(s;3H), 3.9(s;3H), 3.45-3.3(br dt;2H), 2.95-2.8(br s;1H), 1.0(br s;1H)
20	oil	7.7-6.7(m;8H), 3.93(s;3H), 3.85(s;3H), 3.51(br m;2H), 3.21(br m,2H), 0.99(br m;6H)
21	oil	7.7-6.7(m;8H), 3.99(s;3H), 3.87(s;3H), 3.35(br m;2H), 3.18(br m;3H), 1.47(dt;2H), 0.77(t,3H)
22	oil	7.7-6.7(m;8H), 3.95(s;3H), 3.87(s;3H), 3.48(br m;1H), 3.19(br m;1H), 2.91(br s;1H), 2.81(br s;2H), 1.38(br m;2H), 1.1(br m;2H), 0.83(br m;3H)
23	oil	7.7-6.7(m;8H), 3.94(s,3H), 3.84(s,3H), 3.55(br m,2H), 3.25(br m,2H), 1.5(br m;4H), 1.25(br m,2H)

Table 1A (cont'd)

Ex. No.	M.pt (°C)	^{1}H-NMR δ(ppm)
24		7.48-6.68(m;7H), 3.95(s;3H), 3.88(s,3H), 3.75-3.1(br m;8H), 2.45(s;3H)
25		7.5-6.6(m;7H), 3.93(s;3H), 3.88(s;3H), 3.5-3.3(br m;2H), 3.3-3.05(br m;2H), 2.45(s;3H), 0.97(t;6H)
26		7.5-6.6(m;7H), 3.92(s;3H), 3.85(s;3H), 3.4-3.25(br m;1H), 3.25-3.05(br m;1H), 2.95-2.7(br d,3H), 2.45(s;3H), 1.5-1.3(m;2H), 0.8-0.65(br t;3H)
27		7.5(s;1H), 7.3-7.05(m;2H), 7.0-6.9(m;3H), 6.6(s;1H), 4.0(s;3H), 3.9(s;3H), 3.2(m;4H), 2.5(s;3H), 1.4(m;4H), 0.75(t;6H)
28		7.7(d;1H), 7.4(d;1H), 7.3-7.15(m;2H), 7.1-6.9(m;3H), 6.7(s;1H), 4.0;3.9(m;7H), 3.3(q;2H), 1.15(d;6H), 1.0(t;3H)
29		7.7(d;1H), 7.4-7.2(m;3H), 7.0-6.9(m;4H), 4.4(s,2H), 4.0(s;3H), 3.9(s;3H), 3.1(s;3H)
30		7.7(d;1H), 7.3-7.2(m;3H), 7.1(s;1H), 6.95-6.9(m;3H), 4.0(s;3H), 3.9(s;3H), 3.6(s;3H), 3.2(s;3H)
31		7.7(d;1H), 7.4-7.2(m;3H), 7.0(m;3H), 6.8(s;1H), 4.0(s;3H), 3.9(s;3H), 3.8-3.2(br;8H)
32		7.7(d;1H), 7.4-7.15(m;3H), 7.05-6.9(m;3H), 6.7(d;1H), 4.0(s;3H), 3.9(s;3H), 3.7(m;1H), 2.7(s;3H), 1.3(m;2H), 0.9(d;3H), 0.7(m;3H)
33		7.7(d;1H), 7.4-7.2(m;3H), 7.0(m;3H), 6.8(s;1H); 4.0(s;3H), 3.9(s;3H), 3.0(m;5H), 1.6(m;2H), 1.0(m;1H)
34		7.7(d;1H), 7.35-7.1(m;3H), 7.0(m;2H), 6.8(s;1H), 6.3(t;1H), 4.0(m;2H), 4.0(s;3H), 3.8(s;3H)
35		7.45-6.67(m;7H), 3.93(s;3H), 3.84(s;3H), 3.5-3.05(br m;4H), 2.73-2.63(t;2H), 1.7-1.55(m;2H), 1.5-1.3(m;2H), 1.08-0.9(m;9H)

Table 1A (cont'd)

Ex. No.	M.pt (°C)	^{1}H-NMR δ (ppm)
36		7.35-7.2(m;2H), 7.0-6.9(m;4H), 6.7(s;1H), 4.0(s;3H), 3.9(s;3H), 3.5(br;8H)
37		7.35-7.2(m;2H), 7.0-6.9(m;4H), 6.7(s;1H), 4.0(s;3H), 3.9(s;3H), 3.4(m;2H), 3.2(m;2H), 1.0(m;6H)
38		7.5(s;1H), 7.3(d;1H), 7.1(d;1H), 6.95(m;3H), 6.7(s;1H), 4.0(s;3H), 3.9(s;3H), 3.7-3.2(br;8H), 2.8(q;2H), 1.3(t;3H)
39		7.5(s;1H), 7.3(d;1H), 7.1(d;1H), 7.0-6.9(m;3H), 6.7(s;1H), 4.0(s;3H), 3.9(s;3H), 3.9(br;2H), 3.2(br;2H), 2.8(q;2H), 1.3(t;3H), 1.0(t;6H)
40		7.8-6.64(m;7H), 4.11-4.0(q;2H), 3.91(s;3H), 3.85(s;3H), 3.55-3.05(br m;4H), 1.48-1.41(t;3H), 1.0-0.92(t;6H)
41		7.7(d;1H), 7.3-7.15(m;3H), 7.05(s;1H), 6.95(s;3H), 4.0(s;3H), 3.9(s;3H), 3.65(q;2H), 3.6(s;3H), 1.15(t;3H)
42		7.7-6.75(m;7H), 3.95(s;3H), 3.88(s;3H), 3.7-3.1(br m;8H), 1.42(s;9H)
43		7.65-6.65(m;7H), 3.95(s;3H), 3.85(s;3H), 3.5-3.1(br m;4H), 1.4(s;9H), 1.0(t;6H)
44		7.7-6.7(m;8H), 3.93(s;3H), 3.85(s;3H), 3.5-3.05(br m;3H), 1.8-1.6(m;3H), 1.4-1.15(br m;5H), 1.1-1.0(t;3H), 1.05-0.9(br m;2H)
45		7.5(s;1H), 7.25(m;1H), 7.15(d;1H), 6.95(m;3H), 6.75(s;1H), 3.95(s;3H), 3.85(s;3H), 3.45-3.1(br m;8H), 2.7-2.5(m;1H), 2.0-1.8(br m;4H), 1.8-1.7(br m;1H), 1.6-1.2(br m;5H)
46		7.48(s;1H), 7.3-6.85(m;5H), 6.68(s;1H), 3.92(s;3H), 3.85(s;3H), 3.5-3.1(br m;4H), 2.68-2.5(m;1H), 2.0-1.8(br m;4H), 1.8-1.7(br m;1H), 1.6-1.15(br m;5H), 1.05-0.93(t;6H)

Table 1A (cont'd)

Ex. No.	M.pt (°C)	^{1}H-NMR δ(ppm)
47		7.65(d;1H), 7.3-6.8(m;7H), 6.0-5.9(br s;1H), 3.95(s;3H), 3.85(s;3H), 2.8-2.68(m;1H), 0.75(q;2H), 0.48(m;2H)
48		7.68(d;1H), 7.34(d;1H), 7.28-7.1(m;2H), 7.0-6.9(m;3H), 6.83(s;1H), 3.93(s;3H), 3.87(s;3H), 3.5-3.2(br m;2H), 2.5-2.37(br m;1H), 1.08-0.98(t;3H), 0.7-0.5(br m;2H), 0.5-0.3(br m;2H)
49		7.68(d;1H), 7.33(d;1H), 7.3-6.8(m;7H), 3.95(s;3H), 3.85(s;3H), 2.89(br s,3H), 2.55-2.38(br m;1H), 0.7-0.5(br m;2H), 0.5-0.4(br m;2H)
50		7.68-6.83(m;7H), 6.72(s;1H), 3.92(s;3H), 3.88(s;3H), 3.5-3.0(br m;4H), 1.53-1.48(m;2H), 1.09-0.9(br m;2H), 0.9-0.8(t;3H), 0.8-0.7(t;3H)
51		7.68(d;1H), 7.38-6.9(m;6H), 6.72(s;1H), 3.95(s;3H), 3.88(s;3H), 3.5-3.0(br m;4H), 1.46-1.3(m;2H), 1.2-0.72(br m;8H)
52		7.25(m;1H), 7.09(s;1H), 7.0-6.88(m;4H), 6.7(s;1H), 3.93(s;3H), 3.87(s;3H), 3.7-3.1(br m;8H)
53		7.3-6.8(m;6H), 6.63(s;1H), 3.92(s;3H), 3.89(s;3H), 3.86(s;3H), 3.5-3.05(br m;4H), 1.0(t;6H)
54		7.49(s;1H), 7.28-6.85(m;5H), 6.68(s;1H), 3.92(s;3H), 3.88(s;3H), 3.5-3.1(br m;4H), 3.0(m;1H), 1.3(d;6H), 0.98(t;6H)
55		7.5(s;1H), 7.28-7.25(d;1H), 7.14(d;1H), 6.94(d;3H), 6.73(s;1H), 3.96(s;3H), 3.88(s;3H), 3.8-3.1(br m; 8H), 3.0(m;1H), 1.29(d;6H)
56		7.62(s;1H), 7.28-7.1(m;2H), 6.95(m;3H), 6.65(s;1H), 3.92(s;3H), 3.85(s;3H), 3.5-3.05(m;4H), 1.1-0.9(m;6H)
57		7.5-6.9(m;11H), 6.7(s;1H), 5.11(s;2H), 3.95(s;3H), 3.87(s;3H), 3.8-3.1(br m;8H)
58		7.5-6.8(br m;11H), 6.62(s;1H), 5.11(s;2H), 3.9(s;3H), 3.88(s;3H), 3.55-3.05(br m;4H), 1.0(t;6H)

Table 1A (cont'd)

Ex. No.	M.pt (°C)	^{1}H-NMR δ (ppm)
59		7.68(d;1H), 7.35(d;1H), 7.3-7.1(m;2H), 7.05-6.8(m;3H), 6.8-6.6(br s;1H), 4.9-4.6(br m;1H), 4.1-3.95(br m;1H), 3.93(s;3H), 2.9-2.5(br d;3H), 1.1-0.85(br s;6H)
60*		7.63(d;1H), 7.38-7.1(m;5H), 6.76(s;1H), 5.43(br s,2H), 3.65-3.4(br m;8H)
61		7.68(d;1H), 7.4-6.85(m;6H), 6.78(s;1H), 5.8(s;1H), 3.88(s;3H), 3.75-3.1(br m;8H)
62		7.68(d;1H), 7.4-6.8(m;6H), 6.78(s;1H), 6.08(s;2H), 3.9-3.1(br m;8H)
63		7.65(d;1H), 7.33(d;1H), 7.28-7.1(m;4H), 6.9(d;1H), 6.78(s;1H), 3.88(s;3H), 3.8-3.1(br m;8H), 2.25(s;3H)
64		7.65(d;1H), 7.35-7.05(m;5H), 6.85(d;1H), 6.75(s;1H), 4.2(br d;2H), 3.85-3.1(br m;8H)
65		7.65(d;1H), 7.35-6.8(m;6H), 6.78(s;1H), 3.92(br s;2H), 3.75-3.15(br m;8H)
66		7.65(d;1H), 7.5-7.1(m;5H), 6.75(m;3H), 3.85(br s;2H), 3.75-3.0(br m;8H)
67		7.65(d;1H), 7.4-7.0(m;6H), 6.8(s;1H), 3.8-3.1(br m;8H), 2.35(s;3H)
68		7.65(d;1H), 7.35-7.0(m;4H), 6.9(d;1H), 6.75(s;1H), 4.0-3.8(br m;2H), 3.7-3.2(br m;8H)
69		7.9(d;2H), 7.65(d;1H), 7.45(d;1H), 7.4-7.0(m;4H), 6.85(s;1H), 6.4-5.5(br d;2H), 3.8-2.9(br m;8H)
70		8.05(d;2H), 7.62(d;1H), 7.45(d;2H), 7.3(d;1H), 7.3-7.1(m;2H), 6.8(s;1H), 3.7-3.2(m;8H), 2.6(s;3H)
71		7.68(d;1H), 7.35(d;1H), 7.32-6.6(m;6H), 3.8(s;2H), 3.75-3.0(br m;8H), 2.55(q;2H), 1.25(t;3H)

Table 1A (cont'd)

Ex. No.	M.pt (°C)	^{1}H-NMR δ (ppm)
72*		8.76(s;1H), 7.62(d;1H), 7.35-7.05(m;5H), 7.0(d;2H), 6.72(s;1H), 3.6-3.2(br m;8H)
73		7.65(d;1H), 7.3-7.0(m;6H), 6.78(s;1H), 3.96(s;3H), 3.8-3.2(br m;8H)
74		7.8(d;2H), 7.68(d;1H), 7.5(d;2H), 7.4-7.1(m;3H), 6.85(s;1H), 3.9-3.2(br m;8H)
75		7.68(d;1H), 7.48(d;2H), 7.45-7.1(m;5H), 6.8(s;1H), 4.75(d;2H), 3.8-3.0(br m;8H)
76		8.4(d;2H), 7.7(d;1H), 7.58(d;2H), 7.4-7.2(br m;3H), 6.9(s;1H), 3.8-3.2(br m;8H)
77		7.62(d;1H), 7.35(d;1H), 7.3-7.1(m;2H), 6.95(m;3H), 3.92(s;3H), 3.88(s;3H), 3.8-3.0(m;8H), 2.4(s;3H)
78		7.65(d;1H), 7.32(d;1H), 7.3-7.0(m;5H), 6.78(s;1H), 3.75(s;2H), 3.7-3.1(br m;8H), 2.2(s;3H)

NB. ^{1}H-NMR data in Table IA were obtained in $CDCl_3$ at 300 MHz and 20°C except those marked with an asterisk (*) which were obtained in C_3D_6O at 300 MHz and 20°C.

Example 79

6-Chloro-1-(3,4-dimethoxyphenyl)indole-2-carboxylic acid morpholide (compound 9, alternative synthesis)

4-Bromoveratrole (5.7 g, 26 mmol), 6-chloroindole-2-carboxylic acid morpholide (1.7 g, 6.5 mmol), potassium carbonate (1.7 g), copper(I) bromide (0.2 g) in a mixture of pyridine (2 ml) and nitrobenzene was stirred at 140°C for 14 hours. After cooling to room temperature, the reaction mixture was applied onto a flash chromatography column (silica gel, 140 g), Elution with toluene, toluene/acetone [9:1] and toluene/acetone [8:2](500 ml each) gave

6-chloro-1-(3,4-dimethoxyphenyl)indole-2-carboxylic acid morpholide as brown oil. Yield: 2.1 g(81% of theoretical) R_f: 0.54 (toluene/acetone, 7:3) ^{1}H-NMR: δ = 7.6 (d; 1H), 7.3 (s; 1H), 7.15 (d; 1H), 7.0 (m; 2H), 6.9 (s; 1H), 6.7 (s; 1H), 4.0 (s; 3H), 3.9 (s; 3H), 3.7-3.2 ppm (br; 8H).

Example 80

1-(3,4-Dimethoxyphenyl)indole-2-carboxylic acid -N-ethyl isopropyl amide

(compound 28, alternative synthesis)

1-(3,4-Dimethoxyphenyl)indole-2-carboxylic acid (2.0g, 6.8 mmol) was stirred in tetrahydrofuran (10 ml). Triethylamine (1 ml, 7.5 mmol) was added and the mixture was cooled to 0°C. Ethyl chloroformate (0.7 ml, 7 mmol) was added dropwise, followed by stirring for 30 minutes. N-ethyl isopropylamine (0.6 g, 7 mmol) in tetrahydrofuran was added, followed by stirring for 30 minutes and refluxing for 6 hours. The tetrahydrofuran was evaporated *in vacuo*, and the residue was dissolved in toluene. The toluene solution was washed with water, dried, evaporated *in vacuo*, applied onto a flash chromatography column (silica gel, 30 g) and eluted with toluene/acetone (9.5:0.5). The desired fractions were concentrated and the residue triturated with diisopropyl ether to give 1-(3,4-dimethoxyphenyl)indole-2-carboxylic acid N-ethyl isopropyl amide as white crystals which were then filtered and dried. Yield: 50 mg (2% of theoretical). R_f: 0.53 (toluene/acetone 7:3). 1H-NMR: δ (ppm) 7.7 (d;1H), 7.5(d;1H), 7.2(2H), 7.0(1H), 6.7(s;1H), 4.0(7H), 3.3(q;2H), 1.15(d;6H), 1.0(t,3H).

Biological Testing

A) Determination of minimum inhibitory concentration (MIC value):

Ten test tubes (16x160 mm, with aluminum cap, Schott, Mainz, FRG) per compound were filled with nutrient solution (V8-juice, 3ml) and autoclaved. After cooling down, sterile nutrient solution (3ml) containing the active compound (200 µg/ml) was pipetted into

the first tube and mixed. Then, half the content of the first tube (3ml) was transferred to the second tube, mixed and, again, half the content of this tube transferred to the third and so on. By this means, the following series of test solutions was prepared:

Tube No.	1	2	3	4	5	6	7	8	9	10
Concentration (a.i. µg/ml)	100	50	25	12.5	6.25	3.13	1.56	0.78	0.39	0.2

The tubes were inoculated by transferring nutrient agar slices (5 mm diam.) from a <u>Phytophthora</u> <u>infestans</u> <u>agar</u> culture into the tubes. After an incubation time of 7 days at 18°C, the assessment was carried out by visual inspection of the test tubes. The lowest concentration in the test tubes without mycelium growth was recorded as the minimum inhibitory concentration (table 2). All experiments were carried out together with a reference compound 3-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)acrylic acid morpholide).

TABLE 2

Compound Example No.	M.I.C. value	Reference Compound
1	1.56	(0.78)
2	>50	(0.78)
5	>50	(0.78)
8	0.78	(0.39)
9	0.78	(0.78)
13	0.78	(0.78)
18	12.5	(0.78)
19	1.56	(0.39)
20	0.78	(0.78)

Table 2 (cont'd)

Compound Example No.	M.I.C. value	Reference Compound
21	1.56	(0.78)
22	6.25	(0.78)
23	>50	(0.78)
24	1.56	(0.78)
25	0.78	(0.78)
26	1.56	(0.78)
27	>100	(0.39)
28	0.78	(0.39)
29	12.5	(0.39)
30	1.56	(0.39)
31	3.13	(0.78)
32	25	(0.78)
33	6.25	(0.39)
34	>100	(0.78)
35	0.39	(0.78)
36	3.13	(1.56)
37	1.56	(1.56)
38	0.78	(0.78)
39	0.78	(0.78)
40	12.5	(0.78)
41	12.5	(0.78)
42	0.2	(0.78)
43	0.78	(0.78)
44	100	(0.78)
45	3.13	(0.78)
46	100	(0.78)
47	>100	(0.78)
48	6.25	(0.78)
49	1.56	(0.78)
50	12.5	(0.78)
51	6.25	(0.78)

Table 2 (cont'd)

Compound Example No.	M.I.C. value	Reference Compound
52	3.13	(0.78)
53	3.13	(0.78)
55	1.56	(0.78)
56	1.56	(0.78)
57	0.2	(0.78)
58	0.78	(0.78)
59	3.13	(0.78)
60	12.5	(0.78)
61	6.25	(0.78)
62	>100	(0.78)
63	12.5	(0.78)
64	3.13	(0.78)
65	1.56	(0.78)
66	3.13	(0.78)
67	6.25	(0.78)
68	3.13	(0.78)
69	>100	(0.78)
70	>100	(0.78)
71	25	(0.78)
72	>100	(0.78)
73	>100	(0.78)
74	100	(0.78)
75	50	(0.78)
76	>100	(0.78)
77	50	(0.78)
78	3.13	(0.78)

B. Antisporulant activity against vine downy mildew (*Plasmopara viticola*; PVA)

The test is a direct antisporulant foliar spray. The lower surface of leaves of vine plants (cv Cabernet-Sauvignon),

approximately 8 cm high, are inoculated with an aqueous suspension containing 2.5 x 10^4 zoosporangia/ml. The inoculated plants are kept for 24 hours at 21°C in a high humidity cabinet, then 24 hours in the glasshouse at 20°C and 40% R.H. Infected leaves are sprayed on their lower surfaces with the test compound in a 1:1 water/acetone mixture containing 0.04% Tween 20 (Trade mark; a polyoxyethylene sorbitant surfactant) and 600 ppm of the active ingredient. After drying the plants are returned to the glasshouse at 20°C and 40% R.H. for 96 hours and are then transferred to the high humidity cabinet for 24 hours to induce sporulation. The assessment (Table 3) is based on the percentage of the leaf area covered by sporulation compared with that on control leaves according to the below table.

0 = <50 % activity
1 = 50-80 % activity
2 = >80 % activity

C. <u>Direct protectant activity against tomato late blight (Phytophthora infestants; PIP)</u>

The test is a direct protectant foliar spray. Tomato plants with two expanded leaves (cv First in the Field) are sprayed with the test compound as described above. After drying, the plants are kept for 24 hours in the glasshouse at 20°C and 40% R.H. Then, the upper surfaces of the leaves are inoculated with an aqueous suspension containing 2 x 10^5 zoospores/ml. The inoculated plants are kept for 24 hours at 18°C in a high humidity cabinet and 5 days at 15°C and 80% R.H. in a growth chamber with 14 hours light/day. The assessment (Table 3) is based on the percentage of diseased leaf area compared with that on control leaves according to the below Table.

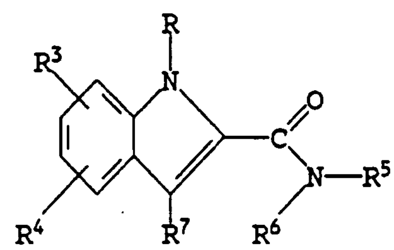
0 = <50 % activity
1 = 50-80 % activity
2 = >80 % activity

Table 3

Compound	PVA	PIP
1	2	2
3	0	0
4	0	0
5	0	0
6	0	0
7	0	0
8	2	2
9	2	2
19	2	2
20	2	2
21	2	2
22	2	2
23	0	0
24	0	2
25	2	2
26	2	2
27	2	2
28	2	2
29	2	2
30	2	2
31	2	2
32	2	1
33	1	2
34	0	0
54		2

CLAIMS

1. A fungicidal composition which comprises a carrier and, as active ingredient, a compound of the general formula



(I)

in which R represents a substituted phenyl group; R^3 and R^4 independently represent a hydrogen or halogen atom or an optionally substituted alkyl, alkoxy, cycloalkyl, phenyl or phenoxy group; R^5 and R^6 independently represent a hydrogen atom or an optionally substituted alkyl, alkoxy, cycloalkyl, phenyl or heterocyclyl group or R^5 and R^6 together with the interjacent nitrogen atom represent a heterocyclyl group; and R^7 represents a hydrogen atom or an alkyl group.

2. A fungicidal composition according to claim 1 in which R represents a phenyl group substituted by one or more substituents selected from halogen atoms, nitro, cyano, hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, hydroxy-C_{1-4} alkyl, amino, C_{1-4} alkanoyl, carbamoyl and C_{1-4} alkylenedioxy groups.

3. A fungicidal composition according to claim 1 or claim 2 in which R^3 and R^4 independently represent a hydrogen or halogen atom or a C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-8} cycloalkyl, phenyl or phenoxy group, each group being optionally substituted by one or more substituents selected from halogen atoms and phenyl groups.

4. A fungicidal composition according to any one of the preceding claims in which R^5 and R^6 independently represent a hydrogen atom, a C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-8} cycloalkyl or phenyl group or a 5- or 6-membered heterocyclic ring or R^5 and R^6 together with the

interjacent nitrogen atom represent a 5- to 6- membered heterocyclic ring, each group or ring being optionally substituted by one or more substituents selected from halogen atoms, cyano, C_{3-6} cycloalkyl, halo-C_{3-6} cycloalkyl and phenyl groups.

5. A fungicidal composition according to any one of the preceding claims in which R^7 represents a hydrogen atom or a C_{1-4} alkyl group.

6. A fungicidal composition according to any one of the preceding claims in which R represents a nitrophenyl, cyanophenyl, hydroxylphenyl, hydroxymethylphenyl, aminophenyl, ethanoylphenyl, carbamoylphenyl, methylenedioxyphenyl, fluoro-methyl-phenyl, fluoro-methoxy-phenyl, fluoro-amino-phenyl, difluoro-amino-phenyl, chloro-amino-phenyl, dichloro-amino-phenyl, hydroxyl-methoxy-phenyl, methyl-methoxy-phenyl, methyl-amino-phenyl, ethyl-amino-phenyl or dimethoxyphenyl group; R^3 represents a hydrogen, fluorine, chlorine or bromine atom or a methyl, ethyl, propyl, butyl, trifluoromethyl, methoxy, ethoxy, propoxy, butoxy, benzyloxy, cyclohexyl, phenyl or chlorophenoxy group; R^4 represents a hydrogen atom; R^5 represents a methyl, ethyl, propyl, butyl, trifluoroethyl, cyanomethyl, dichlorocyclopropylmethyl, benzyl, methoxy, cyclopropyl, cyclohexyl, phenyl or morpholinyl group; R^6 represents a hydrogen atom or a methyl, ethyl or propyl group; or R^5 and R^6 together with the interjacent nitrogen atom represent an imidazolyl, piperidyl or morpholinyl group; and R^7 represents a hydrogen atom or a methyl group.

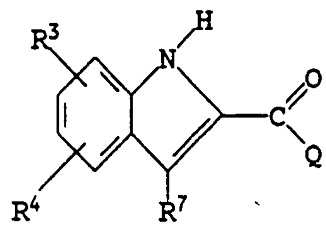
7. A method of combating fungus at a locus which comprises treating the locus with a composition according to any one of claims 1 to 6 or a compound of formula I as defined in any one of claims 1 to 6.

8. The use as a fungicide of a composition according to any one of claims 1 to 6 or a compound of formula I as defined in any one of claims 1 to 6.

9. A compound of the general formula I as defined in claim 1 with the proviso that, when R represents a 2-fluorophenyl group, R^2, R^4, R^5 and R^6 each represent a hydrogen atom and R^7 represents a methyl

group, then R^3 does not represent a chlorine atom substituted at the 5-position of the indole ring.

10. A process for the preparation of a compound of formula I as defined in claim 9 which comprises reacting a compound of the general formula



(II)

in which R^3, R^4 and R^7 are as defined in claim 9 and Q represents a group $-NR^5R^6$ or a group $-OR^8$ where R^5 and R^6 are as defined in claim 9 and R^8 represents an alkyl or alkenyl group, with a compound of the general formula

$$R\text{—}Hal \qquad \text{(III)}$$

in which R is as defined in claim 9 and Hal represents a halogen atom; and, when Q represents a group $-OR^8$ in the compound of formula II, reacting the compound so obtained with a compound of the general formula

$$HNR^5R^6 \qquad \text{(IV)}$$

in which R^5 and R^6 are as defined in claim 9.

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 C07D209/34; A01N43/38; C07D413/06; C07D401/06
C07D413/14

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl. 5	C07D ; A01N

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category °	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No.[13]
X	DE,A,1 935 671 (SUMITOMO CHEMICAL COMPANY LTD.) 5 March 1970 Example 4 wherein the 1 substituent is a halosubstituted phenyl (excluding where it is ortho fluorophenyl). see page 4, line 21 - page 5, line 3 ---	9
X	US,A,3 634 402 (YAMAMOTO) 11 January 1972 Forula (III) in claim 2. see column 13, line 26 - line 27 ---	9
X	EP,A,0 211 698 (SYNTHELAB) 25 February 1987 Examples 37-40, 42-48 and reaction schemes 2 and 3; in particular formula (VI). ---	9

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° Special categories of cited documents : [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
12 AUGUST 1993	17.09.93
International Searching Authority	Signature of Authorized Officer
EUROPEAN PATENT OFFICE	GETTINS M.P.

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category °	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
A	DE,A,1 966 206 (SUMITOMO CHEMICAL COMPANY LTD.) 20 January 1972 Formula (III) on page 4. The compound on page 18 is excluded by the proviso. see page 18, line 1 ---	9
A	DE,A,2 008 692 (AGENCE NATIONALE DE VALORISATION DE LA RECHERCHE (ANVAR)) 17 September 1970 cited in the application see page 4, line 20; claim 1 -----	1-10

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO.

EP 9301406
SA 74842

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
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		FR-A- 2080854	26-11-71
		CH-A- 510017	15-07-71
		GB-A- 1305458	31-01-73

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